

REMARKS

Applicants respectfully request entry of the current amendments to the claims. Applicants believe that the present amendments place all of the claims in condition for allowance, or in a better condition for appeal.

Amendments

Claims 1-40 stand canceled by the present amendment, without prejudice.

Claim 41 has been amended to bring out the feature that the tocopherol compositions of the invention comprise at least 50% gamma-tocopherol. Support for this feature of the invention can be found, for example at page 14, lines 1-9 thereof.

Claim 42 has been amended to bring out the feature that the metabolites of gamma tocopherol are naturally occurring metabolites. Support for this feature of the invention can be found, for example, at page 13, lines 9-13 thereof.

Claim 43 stands canceled by the present amendment, without prejudice.

Claims 53-57 have been amended to conform to the amended language of Claim 42, from which they depend.

Claim 98 has been amended to be an independent claim.

New Claims 99-104 have been added to bring out the feature and embodiment of the invention that gamma-tocopherol compositions in accordance with the present invention comprise less than 20% alpha-tocopherol. Support for this feature of the invention can be found, for example, at page 14, lines 9-14 thereof.

Accordingly, Claims 41, 42, 44-64 and 98-104 are currently pending in the application.

Applicants reserve the right to file the canceled claims and/or subject matter in a one or more continuation applications.

Rejection under 35 U.S.C. 112, first paragraph

A. Claims 2, 11-13, 22, 31-33, 42, 53-57 and 98 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner has indicated that the substitution of the term “naturally occurring metabolite” for the term “natural metabolite” would be considered.

By this amendment, claims 2, 11-13, 22 and 31-33 have been canceled. Claim 42 has been amended to bring out the feature that the claimed metabolites are naturally occurring metabolites of gamma-tocopherol. Claims 53-57 and 98 are dependent upon claim 42, and therefore include the foregoing limitation. Support for this feature of the invention can be found, for example, at page 13, lines 9-13 thereof.

In view of the foregoing amendments, withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is therefore respectfully requested.

B. Claims 3, 5, 7, 8, 24-32, 39-41 and 48-50 stand rejected under 35 U.S.C. 112, first paragraph, on the grounds that the specification does not provide enablement for the use of any metabolite of tocopherol to treat ischemic conditions.

Claims 3, 5, 7, 8, 24-32, 39 and 43 stand canceled by the present amendment.

Applicants thank the Examiner for her telephonic clarification on 16 July 2004 that the claims intended to be included in the foregoing rejection under 35 U.S.C. §112, first paragraph, are those associated with beta-tocopherol metabolites, as summarized in the Office communication mailed 7/19/2004 summarizing the interview. Nonetheless, applicants have made the certain amendments to the remaining claims to better define their invention and, in particular, to delineate among those claims directed to tocopherol compositions and those directed to tocopherol metabolite compositions:

- As stated above, Claim 42 is now directed to the use of a naturally occurring metabolite of gamma- tocopherol, in the method of the invention. Claims 53-57 have been amended to conform to the amended claim language of Claim 42, from which they depend.

- Claims directed to beta- and delta-tocopherol metabolites are canceled by the present amendment, without prejudice.

The test of enablement is whether the applicants have taught how to make and use the invention as claimed.

As a matter of Patent Office practice... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971).

Further the court in *Marzocchi* has stated, “it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” MPEP 2164.04; In re *Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971).

By the present amendment, those claims associated with the use of beta- and delta-tocopherol metabolites have been canceled, without prejudice. Claim 42 has been amended to bring out the feature that anti-ischemic gamma- tocopherol metabolites are naturally occurring metabolites of gamma-tocopherol. Applicants submit that the identities of such metabolites and how to make them are well known in the art. See, for example, applicants’ statement in the instant specification:

“It is well known that gamma-tocopherol is metabolized *in vivo* to form, for example, gamma-CEHC and gamma-CEBC, among other metabolites. In humans, this metabolite is thought to be the result of sequential oxidation of its phytyl sidechain by enzymes that catalyze omega and beta oxidation.” (specification at page 59, lines 17-21)

In addition, applicants have described other tocopherol metabolites, for example at page 22, line 23 to page 23, line 14, of the specification. Further detail is provided, for example, at pages 41-53 of the specification and in the Drawings at Figure 3, where applicants have provided

further, detailed structures of the types of metabolites that are natural by-products of mammalian metabolism of the subject tocopherols. Such compounds are either generally commercially available, or can be produced synthetically by commonly known methods, or can even be isolated from natural sources (see, for example U.S. Patents 6,150,402, 6,083,982, 6,048,891 and 6,242,479, which were specifically incorporated by reference into the instant application).

Furthermore, the applicants have described in detail in the specification how to formulate such compounds into a variety of forms suitable for administration to mammalian subjects, and appropriate routes of administration and dosage schedules for such administration (as described, for example, at page 17, line 9 to page 18, line 20; page 33, line 27 to page 28, line 12; and page 71, line 27 to page 78, line 24 of the specification). Further, the applicants have described in detail how use such formulations to ameliorate the symptoms of certain tissue ischemic conditions, as described, for example at pages page 61, line 14, to page 67, line 28 of the specification.

Accordingly, applicants submit that they have provided sufficient guidance to enable persons skilled in the art to make and use the invention as presently claimed. The Examiner has not provided any documentation or evidence as to why it doubts the truth or accuracy of applicants' assertions in this regard.

In view of the foregoing amendments and remarks, applicants respectfully submit that the instant specification complies with the enablement requirements of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of the objections and rejections thereunder are respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1-64 and 98 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. It is the Examiner's position that the above-referenced claims are rendered indefinite, by virtue of their recitation of phrases such as "a gamma-tocopherol enriched tocopherol composition" or "a gamma-tocopherol metabolite enriched composition."

Claims 1-40 and 43 stand canceled by the present amendment; accordingly, applicants' response is directed to this rejection as it may apply to the remaining claims (41, 42, 44-64 and 98).

Independent claim 41 has been amended to bring out the feature that a "gamma-tocopherol enriched tocopherol composition" refers to tocopherol compositions in which gamma-tocopherol comprise at least 50% of the mixture (*C.f.*, page 14, lines 1 to 27; page 20, lines 17-23).

Independent claim 42, directed to the use of a gamma-tocopherol metabolite compositions, has been amended to bring out the feature that it is the metabolite that is the active ingredient in the composition. Dependent claim 98 is now presented as an independent claim.

Applicants believe that, in view of the foregoing claim amendments, the pending claims are in compliance with the clarity requirements of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of the rejection under this section is respectfully requested.

Rejection under the judicially created doctrine of obviousness-type double patenting

Claims 1-64 and 98 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-62 of co-pending application serial number 10/020,450.

Claims 1-40, and 43 have been canceled by the present amendment. As the Examiner has noted, applicants have requested that this rejection be held in abeyance until the claims of one of the applications are deemed in condition for allowance.

Rejections under 35 U.S.C. 102(e)

A. Claims 1-40 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Wechter, W.J., U.S. 2004/0058987 ("Wechter 2004/0058987").

B. Claims 41-64 and 98 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Wechter, W.J., U.S. 2004/0058986 ("Wechter 2004/0058986").

It is the Examiner's position that the claimed compositions and methods of use of Wechter 2004/0058987 and Wechter 2004/0058986 anticipate the applicants' claimed invention. This rejection is respectfully traversed, in view of the remarks below.

A. Claims 1-40

By the present amendment, claims 1-40 are canceled without prejudice. Accordingly, the rejection of claims 1-40 over Wechter 2004/0058987 is rendered moot for purposes of the presently pending claims.

B. Claims 41-64 and 98

In order to qualify as a prior art reference under 35 U.S.C. §102(e), the reference patent or patent publication must have a filing date that is earlier than the effective filing date of the application under examination. MPEP706.02(a). To sustain a rejection under 35 U.S.C. §102(e), the invention must have been described in application for patent by another filed in the U.S. (or in an international patent application designating the U.S. under 35 U.S.C. §351(a)) before the invention by the applicants.

The Claimed Invention

Claim 43 has been canceled, without prejudice, by the present amendment. Pending claims 41, 42, 44-64 and 98, along with new claims 99-104, are directed to methods of treating and/or ameliorating symptoms of a non-cardiovascular tissue ischemic condition by administering a gamma-tocopherol enriched tocopherol composition comprising at least 50% gamma-tocopherol or a naturally occurring metabolite of gamma-tocopherol. Exemplary tissue ischemic conditions are described in detail in the specification. (see, for example, page 19, line 1 to page 20, line 2 of the Specification).

Wechter 2004/0058986

Wechter 2004/0058986 was filed on September 12, 2003 and claims priority via a series of continuation applications to December 17, 1998.

The specification of Wechter 2004/0058986 describes the use gamma-tocopherol, to treat a number conditions: "high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathological lesions and a reduced immune

system response...” (Paragraph [0008]); “producing a natriuretic effect” (Paragraph [0009]); “cardiovascular diseases such as ischemia, angina, edematous conditions, atherosclerosis, LDL-oxidation, adhesion of monocytes to endothelial cells, foam cell formation, fatty-streak development, platelet adherence, platelet aggregation, smooth muscle cell proliferation, and reperfusion injury....treat and prevent cancers such as lung cancer, prostate cancer, breast cancer, and colon cancer” (Paragraph [0011]); “treatment and prevention of natriuretic diseases, such as hypertension, high blood pressure, ischemia, angina pectoris, congestive heart failure, cirrhosis of the liver, nephritic syndrome, ineffective renal perfusion or ineffective glomerular filtration....neurological diseases including hyporeflexia, ophthalmoplegia, and axonal dystrophy... improve a subject’s immune system response, reduce the production of free radicals...” (Paragraph [0012]).

While, as exemplified above, the specification of Wechter 2004/0058986 describes the use of gamma-tocopherol for treating a whole plethora diseases, nowhere in the specification of Wechter 2004/0058986 is the term “non-cardiovascular tissue ischemia” used. Furthermore, none of the diseases listed by Wechter 2004/0058986 appear to fall into the category of diseases that the applicants have defined as “non-cardiovascular tissue ischemia,” or, for that matter, that persons skilled in the art would categorize in such a manner.

For what appears to applicants to be the first time in the string of applications in the patent family that encompasses Wechter 2004/0058986, applicant Wechter introduces the term “non-cardiovascular tissue ischemia” into the claims of the application.

Analysis

1. The claims of Wechter 2004/0058986 are not supported by the disclosure of the specification.

Although Wechter 2004/0058986 claims priority to earlier filed continuation applications, the specification on which Wechter 2004/0058986 is based does not support its claims, as described above. Accordingly, the claims and the subject matter thereof cannot derive benefit of the earlier filing date(s). Thus, since filing date of Wechter 2004/0058986 is later than both the filing date and the priority dates of the applicants’ instant application, the subject matter of

Wechter 2004/0058986 that the Examiner has cited against the instant claims cannot be said to anticipate the applicants' claimed invention.

2. Rejection under 35 U.S.C. §102(e) is improper.

Furthermore, a rejection under 35 U.S.C. §102(e) is improper if the Examiner believes that the claims of Wechter 2004/0058986 are identical to the claims of the instant application. In such instances, the Examiner must determine whether a double patenting rejection or an interference is appropriate. MPEP 706.02(b). In the current case, there is no support in the specification for the claims as filed in Wechter 2004/0058986.

In view of the foregoing, applicants submit that Wechter 2004/0058986 is not an effective reference against the applicants' pending claims. Accordingly, withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Rejection under 35 U.S.C. 103(a)

Claims 1-64 and 98 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Wechter, W.J., U.S. 2004/0029954 ("Wechter 2004/0029954"). It is the Examiner's position that the claims of Wechter 2004/0029954 "directed to methods of treating or preventing any ischemic condition...includ[ing] those associated with the liver, the kidney, diabetes, thromboembolytic disease, the brain, the nervous system and the eye" using gamma-tocopherol or a metabolite (LLU- α) of gamma-tocopherol render obvious the applicants' claimed invention.

The Claimed Invention

Claim 43 has been canceled, without prejudice, by the present amendment. Pending claims 41, 42, 44-64 and 98, along with new claims 99-104, are directed to methods of treating and/or ameliorating symptoms of a non-cardiovascular tissue ischemic condition by administering a gamma-tocopherol enriched tocopherol composition comprising at least 50% gamma-tocopherol or a naturally occurring metabolite of gamma-tocopherol.

The Cited Reference

Wechter 2004/0029954 was filed on February 21, 2003 and claims priority via a series of continuation applications to December 17, 1998. Except for the claims, applicants submit that

the specification of Wechter 2004/0029954 is essentially identical to that of Wechter 2004/0058986, described above. As stated above, while the specification of Wechter 2004/0029954 describes a whole “laundry list” of maladies, it does not describe or support the subject matter of the claims set forth in the application as filed on February 21, 2003, which form the basis for the Examiner’s rejection under this section.

Analysis

1. Wechter 2004/0029954 is not an effective reference against the instant application for the subject matter cited by the Examiner.

As stated above, the subject matter of Wechter 2004/0029954 that the Examiner cites against the applicants’ claimed invention is not supported by the specification and therefore does not derive the benefit of the earlier filing date(s). Specifically, the filing date of Wechter 2004/0029954 is later than both the filing date and the priority dates of the applicants’ instant application, the cited subject matter of Wechter 2004/0029954 cannot be said to render obvious the applicants’ claimed invention.

2. Wechter 2004/0029954 does not render obvious the claimed subject matter of the instant application.

The subject matter of the specification of Wechter 2004/0029954 is described in the previous section. To re-iterate, Wechter 2004/0058986 describes the use gamma-tocopherol, to treat a number conditions: “high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathological lesions and a reduced immune system response...” (Paragraph [0008]); “producing a natriuretic effect” (Paragraph [0009]); “cardiovascular diseases such as ischemia, angina, edematous conditions, atherosclerosis, LDL-oxidation, adhesion of monocytes to endothelial cells, foam cell formation, fatty-streak development, platelet adherence, platelet aggregation, smooth muscle cell proliferation, and reperfusion injury....treat and prevent cancers such as lung cancer, prostate cancer, breast cancer, and colon cancer” (Paragraph [0011]); “treatment and prevention of natriuretic diseases, such as hypertension, high blood pressure, ischemia, angina pectoris, congestive heart failure, cirrhosis of the liver, nephritic syndrome, ineffective renal perfusion or

ineffective glomerular filtration....neurological diseases including hyporeflexia, ophthalmoplegia, and axonal dystrophy... improve a subject's immune system response, reduce the production of free radicals..." (Paragraph [0012]).

Analysis

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (MPEP 2143).

While Wechter 2004/0029954 suggests the use of gamma-tocopherol for a whole plethora of indications, these indications would not fall into the category of non-cardiovascular tissue ischemias. Nor is there anything in the reference that would suggest that its teachings of the treatment of the various enumerated disease states might also be applicable to treating non-cardiovascular tissue ischemias.

Since the reference neither shows nor suggests methods of treating non-cardiovascular ischemia, along the lines of the applicants' claimed invention, it cannot be said to render obvious the instant invention. Accordingly, reconsideration and withdrawal of the rejection of the claims over Wechter 2004/0029954 is respectfully requested.

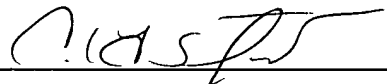
CONCLUSION

Applicants believe that the instant application is now fully in condition for allowance. Early notice to that effect is respectfully requested. If a telephone conversation would expedite the prosecution of this application, the Examiner is invited to contact the undersigned at the telephone number provided below.

If the Patent Office determines that the instant Reply and Amendment requires additional fee(s), the Commissioner is hereby authorized to charge Deposit Account No. 50-2859. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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